

AMENDMENTS TO THE CLAIMS

1. (Currently amended) A method of identifying the presence or absence of at least one ~~of a plurality of preselected polymorphisms that may be present in a~~ cytochrome P450 2D6 polymorphism gene sequence in a sample, the method comprising:

(a) amplifying a cytochrome P450 2D6 gene sequence from the sample using multiplex amplification primers comprising SEQ ID NOs: 1-4; and

(b) identifying the presence or absence of a cytochrome P450 2D6 polymorphism in the gene sequence amplified in step (a) using a primer extension reaction comprising a plurality of extension primers and a set of distinctively labeled ddNTPs.

~~(a) — incubating a reaction comprising:~~

~~—— (i) — an amount of nucleic acid obtained from said sample sufficient for primer extension, wherein said nucleic acid comprises said P450 2D6 gene sequence,~~

~~(ii) — a nucleic acid polymerase,~~

~~(iii) — a plurality of extension primers that specifically bind to a P450 2D6 gene sequence and that, when extended by one nucleotide at the 3' end, comprise a nucleotide indicative of one of a plurality of preselected polymorphisms in said P450 2D6 gene sequence, and~~

~~(iv) — a set of distinctively labeled ddNTPs,~~

~~under conditions such that at least one of said extension primers is distinctively labeled by addition of one of said labeled ddNTPs to the 3' end of said at least one of said extension primers, to generate at least one labeled nucleic acid corresponding to at least one of said preselected polymorphisms; and~~

~~(b) — using said at least one labeled nucleic acid to identify the said at least one of a plurality of preselected polymorphisms present in a cytochrome P450 2D6 gene sequence in the nucleic acid sample.~~

- 2.-3. (Canceled)
4. (Currently amended) The method of claim 1, wherein ~~said using~~ step (b) comprises mobilizing said at least one labeled nucleic acid by electrophoresis.
5. (Original) The method of claim 4, wherein said electrophoresis is capillary electrophoresis.
6. (Previously presented) The method claim 1, wherein one or more of steps (a) or (b) are automated.
7. (Original) The method of claim 1, wherein said distinctive labeled ddNTPs are fluorescently labeled.
8. (Currently amended) The method of claim 1, wherein said ~~one of a plurality of preselected polymorphisms in said cytochrome~~ P450 2D6 polymorphism ~~gene sequence~~ is selected from the group consisting of a duplication, a deletion, an inversion, an insertion, a translocation, a polymorphism resulting in aberrant RNA splicing, and a single nucleotide polymorphism.
9. (Currently amended) The method of claim 1, wherein said preselected at least one of cytochrome P450 2D6 polymorphisms ~~are is~~ selected from the group consisting of CYP2D6*3, CYP2D6*4, CYP2D6*5, CYP2D6*6, CYP2D6*7, CYP2D6*8, CYP2D6*10, CYP2D6*17 and CYP2D6*Nx2.
10. (Currently amended) The method of claim 9, wherein at least one of said extension primers ~~have sequences~~ comprises a sequence selected from the group consisting of SEQ ID NOS: 9 through 19.
11. (Original) The method of claim 1, wherein said sample is a human sample.

12. (Currently amended) The method of claim 1, wherein said ~~one of a plurality of polymorphisms~~ **cytochrome 2D6 polymorphism** is associated with a phenotype selected from the group consisting of having a reduced rate or degree of metabolism of one or more xenobiotics or endobiotics, an increased rate or degree of metabolism of one or more xenobiotics or endobiotics, a decreased or increased specificity for one or more xenobiotics or endobiotics, and combinations thereof.

13. (Previously presented) The method of claim 12, wherein said one or more xenobiotics is a toxin, a carcinogen or a narcotic, or a metabolic precursor thereof.

14. (Original) The method of claim 13, wherein said sample is a sample from a subject having a genetic predisposition to suffer from a toxin, a carcinogen, or a narcotic.

15. (Previously presented) The method of claim 12, wherein said one or more xenobiotics is a therapeutic drug or a metabolic precursor thereof.

16. (Original) The method of claim 15, wherein said therapeutic drug is a cardioactive drug or a psychoactive drug.

17. (Original) The method of claim 15, wherein said subject has a disease or disorder that may be treated by said therapeutic drug.

18. (Original) The method of claim 1, further comprising detection of wildtype P450 2D6.

19.-29. (Canceled)

30. (Currently amended) A method of selecting a therapeutic drug, or a prodrug thereof, to treat a subject suffering from a disease or disorder, said method comprising:

determining the cytochrome P450 2D6 genotype of a subject by the method of claim 1 or 36; and

selecting said therapeutic drug or prodrug to be compatible with ~~a cytochrome P450 2D6~~ said genotype ~~of said subject identified by the method of claim 1 or 19.~~

31. (Currently amended) A method of selecting a dosage of a therapeutic drug, or a prodrug thereof, to treat a subject suffering from a disease or disorder, said method comprising:
determining the cytochrome P450 2D6 genotype of a subject by the method of claim 1 or 36; and

selecting said dosage to be compatible with ~~a cytochrome P450 2D6~~ said genotype ~~of said subject identified by the method of claim 1 or 19.~~

32. (Previously presented) The method of claim 31, wherein said P450 2D6 genotype of said subject comprises a cytochrome P450 2D6 gene selected from the group consisting of CYP2D6*3, CYP2D6*4, CYP2D6*5, CYP2D6*6, CYP2D6*7, CYP2D6*8, CYP2D6*10, CYP2D6*17 and CYP2D6*Nx2.

33.-35. (Canceled)

36. (Currently amended) A method of identifying the presence or absence of at least one ~~of a preselected polymorphisms that may be present in a~~ cytochrome P450 2D6 polymorphism gene sequence in a **human** sample, the method comprising:

(a) amplifying a cytochrome P450 2D6 gene sequence using multiplex amplification primers comprising SEQ ID NOs: 5-8; and

(b) identifying the presence or absence of a cytochrome P450 2D6 polymorphism in the gene sequence amplified in step (a) using a primer extension reaction comprising a plurality of extension primers and a set of distinctively labeled ddNTPs.

~~(a) incubating a reaction comprising:~~

~~—— (i) — an amount of nucleic acid obtained from said sample sufficient for primer extension, wherein said nucleic acid comprises said P450 2D6 gene sequence,~~

(ii) ~~— a nucleic acid polymerase,~~
(iii) ~~— at least one extension primer selected from the group~~
~~consisting of SEQ ID NOs 9 to 19, and~~
(iv) ~~— a set of distinctively labeled ddNTPs,~~
~~under conditions such that said at least one extension primer is distinctively~~
~~labeled by addition of one of said distinctively labeled ddNTPs comprising a label to~~
~~the 3' end of said at least one extension primer, to generate at least one labeled~~
~~nucleic acid corresponding to at least one of said preselected polymorphisms; and~~
(b) ~~— using said at least one labeled nucleic acid to identify the said at least~~
~~one of a plurality of preselected polymorphisms present in a cytochrome P450 2D6~~
~~gene sequence in the nucleic acid sample.~~

37.-38. (Canceled)

39. (Currently amended) The method of claim 36, wherein ~~said using~~ step (b) comprises mobilizing said at least one labeled nucleic acid by electrophoresis.

40. (Original) The method of claim 39, wherein said electrophoresis is capillary electrophoresis.

41. (Previously presented) The method claim 36, wherein one or more of steps (a) or (b) are automated.

42. (Original) The method of claim 36, wherein said distinctive labeled ddNTPs are fluorescently labeled.

43. (Withdrawn, Currently amended) The method of claim 36, wherein said **plurality of extension** primers **are comprise primers comprising the sequences of each of** SEQ ID NO: 17, 18 and 19.

44. (Currently amended) The method of claim 36, wherein **at least one of** said **plurality of** extension primers **comprise the sequence of** SEQ ID NO: 11.

45. (Currently amended) The method of claim 36, wherein said **plurality of** extension primers **comprise primers comprising the sequences of** ~~are~~ SEQ ID NO: 11 and 14.

46. (Previously presented) The method of claim 30, wherein said P450 2D6 genotype of said subject comprises a cytochrome P450 2D6 gene selected from the group consisting of CYP2D6*3, CYP2D6*4, CYP2D6*5, CYP2D6*6, CYP2D6*7, CYP2D6*8, CYP2D6*10, CYP2D6*17 and CYP2D6*Nx2.

47. (New) The method of claim 36, wherein at least one of said extension primers comprises a sequence selected from the group consisting of SEQ ID NOs: 9 through 19.

48. (New) The method of claim 36, wherein said sample is a human sample.